

Remarks

This reply responds to the Final Office Action mailed March 3, 2010. Claims 29-40 are pending, with claims 30, 33, and 35-40 being withdrawn from consideration.

During a May 19, 2010 telephone interview, the Examiner indicated that the restriction requirement and rejections of record would be withdrawn upon presentation of a written response to the Final Office Action and the application, including all pending claims would be allowed and proceed to issue.

Reconsideration of the rejections of record, rejoinder of the withdrawn claims, and allowance of the application in view of the following remarks are therefore respectfully requested.

Statement of Interview

Applicants express appreciation for the courtesies extended by the Examiner Robert Havlin during a May 20, 2010 telephone interview with Applicants' representatives Arnold Turk and Adaku Nwachukwu.

During the telephone interview, Applicants' representatives presented arguments as to the fact that there is no motivation or reason for one having ordinary skill in the art to pick compound 177 disclosed in WO 03/051854 (referred to as "Murakata" hereinafter, which published as U.S. Published Application 2006/0074113 A1, and which issued as U.S. Patent No. 7,425,636) as a lead compound. Applicants' representatives indicated that Murakata discloses a number of compounds having GI_{50} values of 1 μ mol/L or lower (see U.S. Patent No. 7,425,636, page 22, paragraphs [0355] to [0357], and in Table 14) for inhibition of cancer cell proliferation, and compound 177 is not referenced in this list. Applicants' representatives argued that one of

ordinary skill in the art would, at most, choose one of the compounds listed in Table 14, and would not choose compound 177 as a lead compound. Applicants' representatives brought the Examiner's attention to *Takeda Chem. Indus. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1356 (Fed. Cir. 2007), which was presented in the response to the previous Office Action.

Applicants' representatives additionally argued that even if for the sake of argument compound 177 was modified, there is no motivation to add –CH₂ at any particular position in compound 177. Applicants' representatives noted that Silverman does not provide any teaching or suggestion for specifically choosing the location of compound 177 asserted in the rejections of record. Moreover, it was noted that Applicants' claimed compound has activity as a mitotic kinesin Eg5 inhibitor.

The Examiner indicated that the arguments were persuasive and the elected species, compound 237, would be allowed. The Examiner indicated that he would perform a further review of the prior art regarding the non-elected species, i.e., compound 221, and would contact Applicants' representatives regarding this further review. Later in the day, the Examiner contacted Applicants' representatives to indicate that the non-elected species of compound 221 was also allowable, and that the non-elected species and non-elected method claims would be rejoined, and would also be allowed.

Restriction Requirement

Claims 29, 31, 32 and 34 are under prosecution as being directed to an elected species and invention, and claims 30, 33 and 35-40 stand withdrawn from consideration as being drawn to non-elected subject matter.

In response and pursuant to the above-discussed May 19, 2010 telephone interview with the Examiner, Applicants request rejoinder of non-elected species of compound 221 and the non-elected Group II method claims, so that each of pending claims 29-40 will be under consideration and allowed.

Response to Claim Rejection Under 35 U.S.C. § 103

Claims 29, 31, 32, and 34 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Murakata et al. (WO 03/051854, abstract from CAPLUS Accession # 2003:491200 and English language equivalent U.S. Published Application 2006/0074113 A1) in view of Silverman (The Org. Chem. of Drug Design and Drug Action, (1992), pages 4-51).

Applicants note that during the above-noted May 20, 2010 telephone interview, the Examiner indicated that this ground of rejection would be withdrawn. In particular, the Examiner agreed that there is no reason to choose compound 177, disclosed in Murakata, as a lead compound, that there is no reason to modify or combine the teachings as asserted in the rejection, and that there is no expectation of success in the modification or combination.

As discussed during the interview, Murakata discloses a vast number of compounds and there is a lack of motivation to pick and choose any compound, let alone the compound asserted in the rejection, in an attempt to arrive at Applicants' claimed subject matter. In particular, Murakata teaches general formula (I) containing different types of functional groups, as recited in Tables 1-13, which encompasses a large number of structurally varied compounds. Furthermore, there is nothing in Murakata that provides a reason for one of ordinary skill in the art to choose Compound 177 to modify or combine with the teachings of Silverman.

Applicants' note Murakata discloses a number of compounds having GI₅₀ values of 1 μ mol/L or lower for inhibition of cancer cell proliferation, and compound 177 is not referenced in this list. Applicants' submit that one of ordinary skill in the art would at most choose one of the compounds listed in Table 14 as a lead compound, and would not choose compound 177 as a lead compound.

Applicants remind the Examiner that in order to establish a *prima facie* case for obviousness with regard to a novel compound, the motivation of one skilled in the art to conduct a chemical modification of a known compound in a particular manner is important. For example, in *Takeda Chem. Indus. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1356 (Fed. Cir. 2007), the Court states that:

[n]ormally a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound." That is so because close or established "[s]tructural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds." *In re Deuel*, 51 F.3d 1552, 1558 (Fed. Cir. 1995). A known compound may suggest its homolog, analog, or isomer because such compounds "often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties." *Id.* We clarified, however, that in order to find a *prima facie* case of unpatentability in such instances, a showing that the "prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention" was also required. *Id.* (citing *In re Jones*, 958 F.2d 347 (Fed. Cir. 1992); *Dillon*, 919 F.2d 688; *Grabiak*, 769 F.2d 729; *In re Lalu*, 747 F.2d 703 (Fed. Cir. 1984)).

(Emphasis added).

The Court further states that this "test for *prima facie* obviousness for chemical compounds is consistent with the legal principles enunciated in *KSR*." *Id.* The Court also says that "cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular

manner to establish prima facie obviousness of a new claimed compound.” (Emphasis added). *Id.* at 1357.

In analyzing the lower court’s rationale, the Federal Circuit stated that “[w]ith regard to homologation, the [lower] court found nothing in the prior art to provide a reasonable expectation that adding a methyl group to compound b would reduce or eliminate its toxicity.” *Id.* at 1360.

A similar situation is present here wherein Applicants’ claimed subject matter is not rendered obvious by the prior art. There is no reason present in the disclosure of Murakata to arrive at the compounds recited in Applicants’ claims. There must be some motivation to pick and choose specific compounds from amongst the diverse compounds disclosed in Murakata, and then to modify such compounds in a specific manner as asserted in the rejection.

In the instant situation, the rejection has not established any reason for picking and choosing the compound 177 let alone any reason for modifying this compound in any specific manner. Thus, one having ordinary skill in the art would not have chosen compound 177, and would not have sought to modify compound 177 by adding CH₂ at any particular location of this compound. Similarly, Silverman fails to provide a reason to modify any particular compound in Murakata by adding CH₂ at a particular location. Further, there is no reason to combine the teachings of Murakata and Silverman to add CH₂ at any particular location of a compound in Murakata.

Still further, while there is no motivation to make the combination of Murakata and Silverman asserted in the rejection, Applicants further note that there are various locations on compound 177 where a CH₂ group can be added. However, neither

Murakata nor Silverman provides guidance as to any particular location where the CH₂ group should be added. Thus, the rejection uses improper hindsight in an attempt to arrive at Applicants' claimed compound.

Still further, the rejection contends that Silverman teaches lengthening a carbon chain by increasing successive CH₂ groups increases pharmacological effects. Applicants note that the introduction of molecules, such as CH₂, to a compound would be expected to affect the conformational structure of the compound. In fact, introduction of molecules can result in significant three-dimensional conformational changes that can affect the pharmacological activity of a compound. Applicants submit that for this additional reason there is no expectation of success in modifying Murakata in view of Silverman to arrive at compounds with increased pharmacological activity.

In view of the foregoing, and the interview of May 20, 2010 where the Examiner indicated that claims 29-40 are allowable, Applicants respectfully request that the rejection of claims 29, 31, 32, and 34 should be withdrawn.

Response to Claim Rejection Under Non-Statutory Obviousness-Type Double Patenting

Claims 29, 31, 32, and 34 are rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 7,425,636 in view of Silverman.

Applicants initially note that U.S. Published Patent Application 2006/0074113 A1, which is referenced in the prior art rejection discussed above, issued as U.S. Patent No. 7,425,636.

Applicants also note that the rejection indicates that claims 13-17, 22, and 23 are rejected on the ground of nonstatutory obviousness-type double patenting. However, it is apparent that

the rejection intended to reject claims 29, 31, 32, and 34 on the grounds of nonstatutory obviousness-type double patenting because claims 13-17, 22, and 23 have been canceled. Therefore, the arguments presented below are made with respect to claims 29, 31, 32, and 34.

Moreover, as noted above, during the above-noted telephone interview, the Examiner indicated that this ground of rejection would be withdrawn at least for the reasons set forth with respect to the obviousness rejection. Accordingly, withdrawal of this ground of rejection is respectfully requested.

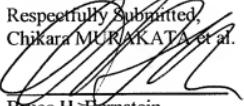
CONCLUSION

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the restriction requirement and rejections of record, and allow each of the pending claims.

Applicants therefore respectfully request that an early indication of allowance of the application be indicated by the mailing of the Notices of Allowance and Allowability.

Should the Examiner have any questions regarding this application, the Examiner is invited to contact the undersigned at the below-listed telephone number.

Respectfully Submitted,
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